UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,234	09/25/2006	Stephen Robert Wedge	056291-5304	1864

9629 7590 04/30/2009

MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
04/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,234	WEDGE, STEPHEN ROBERT	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 and 12-24* is/are pending in the application.

4a) Of the above claim(s) *12-18 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 12/18/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Status of the Claims

Claims 10, 12-24 are currently pending in this application.

Claims 12-18, and 24 withdrawn for being directed to non-elected subject matter.

Claims 10, 19-23 are presently under examination.

Declaration under 37 CFR 1.132

It is noted that the declaration of Stephen R. Wedge, received 02/13/09, has been considered but is not found to be sufficient to overcome the rejection of record for the following reason:

The scope of the declaration is not commensurate with the scope of the instant claims in view of the fact that the data relied upon by declarant show that the growth of inhibition of tumors observed when AZD2171 was administered orally in a dose of 3 mg/kg or 1.5 mg/kg in combination with intravenously administered docetaxel in a dose 10 mg/kg was significantly greater with the combination than when either AZD2171 or docetaxel was used alone; however, the instant claims do not require a specific dose amount of either agent or a specific route of administration. Thus, the declaration is not

found be sufficient to overcome the rejection under 103(a) because the scope of the declaration is not commensurate in scope with the scope of the instant claims.

Further, the data relied upon by declarant only show that the combination of AZD2171 and docetaxel is superior to either drug alone; however, instant claim 10, for example, encompasses combinations of AZD2171 and a taxane. Since the instant claims encompass combinations comprising AZD2171 in combination with any taxane, the scope of the declaration is not found to be commensurate with the instant claims in view of the fact that the data relied upon by declarant is limited to only combinations of AZD2171 and docetaxel.

Response to applicant's arguments

Claim Objection

This objection is withdrawn in view of the claim amendment.

Rejection under 112 2nd. paragraph

This rejection is withdrawn in view of the claim amendment.

Rejection under 102(b)

This rejection is withdrawn in view of applicant's persuasive argument (see applicant's Response, pages 6-11).

REJECTIONS

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10 and 19, 21-23 are rejected under 103(a) as being unpatentable over Stokes et al. (WO 00/47212; equivalent to US Patent 7,074,800), as evidenced Li et al. (US Patent 5,977,163).

Stokes et al. (US Patent 7,074,800) teach compositions comprising certain angiogenesis inhibitors, including AZD2171, or a pharmaceutically acceptable salt thereof, in association with a pharmaceutically acceptable excipient or carrier (see abstract and reference claim 12). Stokes et al. teach antiangiogenic compounds, including AZD2171 (see reference claim 12), or pharmaceutically acceptable salts, for use in the manufacture of medicament for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal such as a human being (see also

col. 62, lines 1-35). Stokes et al. teach that in the field of oncology, it is normal practice to use a combination of different forms of treatment to treat each patient with cancer (col. 62, lines 42-45). Stokes et al. teach that conjoint treatment with surgery, radiotherapy or chemotherapy may be achieved by way of the simultaneous, sequential or separate administration of the individual components of the treatment (col. 62, line 36 to col. 63, line 32, especially, col. 62, lines 40-42). In particular, Stokes et al. disclose antiproliferative/antineoplastic agents such as taxoid like taxol and taxotere (also known as docetaxel) to be suitable for use in combination with said antiangiogenic compounds (col. 63, lines 11-32, especially line 23).

The above discussion of Stokes et al. is incorporated by reference. However, Stokes et al. do not expressly teach that docetaxol is the same as taxotere.

Li et al. (US Patent 5,977,163) is added as an evidentiary reference only for its teaching that taxotere as taught by Stokes et al. is also known as docetaxel (abstract).

It would have been obvious to a person of skill in the art at the time the invention was made to combine any compound species of formula 1, including applicant's claimed compound, with any suitable conventionally known antiproliferative/ antineoplastic drug (e.g. taxotere), and a pharmaceutically acceptable excipient or carrier as taught by Stokes et al. for additive therapeutic effects (col. 63, lines 11-27; see also reference claims 12 and 25). One would have been motivated to do so because Stokes et al. suggest that compounds of formula I, including applicant's claimed compound, may be combined with any known suitable antiproliferative/antineoplastic agent (e.g. taxotere; col. 63, line 23). The motivation for

combining the components flows from their individually known common utility (see In re Kerkhoven, 205 USPQ 1069 (CCPPA 1980).

Regarding claims 10, 19, and 21, Stokes et al. teach AZD2171 free base and pharmaceutically salts thereof (reference claim 12).

Regarding claims 22-23, Stokes et al teach taxotere, which is also known as docetaxel as evidenced by the teaching of Li et al. (abstract).

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Claim 20 is rejected under 103(a) as being unpatentable over Stokes et al. (WO 00/47212; equivalent to US Patent 7,074,800), as evidenced Li et al. (US Patent 5,977,163) in view of Penkler et al (6,255,502).

The above discussion of Stokes et al. is incorporated by reference. However, Stokes et al. do not teach maleate salt.

Penkler et al. teach compositions comprising pharmaceutical actives capable of existing in both free base and acid addition salt form, wherein the acids used include hydrochloride, and maleate salts (col. 2, lines 38-42).

It would have been obvious to a person of skill in the art at the time the invention was made to combine the teachings of the cited references to select any suitable acid addition salt of AZD2171, including applicant's maleate salt, for use in a pharmaceutical composition. One would have been motivated to do so because Penkler et al. suggest

acid addition salts forms (e.g. maleate and hydrochloride) can be prepared for compounds that are capable of existing in both free base and acid addition salt form (col. 2, lines 38-42) and Stokes et al. teach that compounds (e.g. AZD2171) that are capable of existing in both the free base and acid addition salt form (e.g. hydrochloride salt; col. 46, line 55 and reference claim 12) such that one would reasonably expect to successfully prepare a maleate salt form of AZD2171 for use in a composition as taught by Stokes et al. since both maleate and hydrochloride salts are acid addition salts as evidenced by the teaching of Penkler et al. (col. 2, lines 38-42).

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Response to applicant's arguments

Rejection under 103 (a)

Applicant's argument that it would not have been obvious to a person of skill in the art at the time the invention was made to combine AZD2171 and a taxane (i.e. docetaxel) because no where in Stokes does it state that use of any compound of the invention therein with other treatments will produce surprisingly beneficial effects is not found to be persuasive in view of the fact that applicant's argument is not commensurate with the scope of the instant claims. The above discussion in connection with the declaration of Stephen R. Wedge is incorporated by reference.

Applicant's argument that Stokes et al. describes many compounds of formula I, of which AZD2171 is but one, and fails to provide guidance regarding the conjoint

treatment for the combination of any particular compound of formula I with any particular disclosed chemotherapeutic agent (col. 63, lines 34-39) is not found to be persuasive because it is routine in the oncology art to combine two or more compounds for use in the treatment of cancer and Stokes et al. suggest that compounds of formula I, including AZD2171, may be combined with another antiprolliferative/antineoplastic drug and docetaxel as disclosed by Stokes et al. is a conventionally known antiproliferative/antineoplastic agent (col. 63, lines 11-23) such that one would reasonably expect to successfully combine any compound species of formula I (e.g. AZD2171) with any suitable conventionally known antiproliferative/antineoplastic agent (e.g. docetaxel) for use in a composition to treat cancer and applicant (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. …, 82 USPQ2d 1385 (2007). With regards to applicant's assertion of unexpected results with the combination of AZD2171 and a taxane, as discussed above in connection with the declaration of Stephen R. Wedge, the instant claims are not commensurate in scope with the instant claims and therefore applicant's assertion of unexpectedly results is not found to be sufficient to overcome the rejection under 103(a).

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10, 19-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 7 of copending application 10/563,439, in view of Ple (US Patent 7,462,623).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

It is noted that the reference claims are directed to compositions comprising AZD2171, or a pharmaceutically salt thereof, in combination with AZD1839 and a pharmaceutically acceptable carrier or excipient. Unlike the instant claims, the reference claims of the above copending application are not directed to combinations comprising taxane compounds (i.e. taxotere).

Ple teaches anti-tumor quinazoline derivative compounds which are useful in methods of treating solid tumors in humans or animals (col. 1, lines 4-13). Ple states that said compounds may be applied as a sole therapy or may involve, in addition to the quinazoline derivative compound, conventional surgery or radiotherapy or chemotherapy (col. 3, lines 53-56; col. 43, lines 22-58). Ple teach that the chemotherapy may include one or more categories of anti-tumor agents, including antiproliferative/antineoplastic drugs and combinations thereof (e.g. taxoids like taxol and taxotere; col. 43, lines 31-44); …, and inhibitors of growth factor function (e.g. gefitnib, ZD1839).

It would have been obvious to a person of skill in the art at the time the invention was made to manipulate the reference combination of AZD2171 and ZD1839 by substituting the ZD1839 with any conventionally known chemotherapy (e.g.taxotere) as taught by Ple (col. 43, line 44) to arrive at the instant claimed invention (AZD2171 in

combination with taxotere) for use in treating solid tumors in humans. One would have been motivated to do so because Ple suggest that quinoazoline derivative compounds with anti-tumor activity can be combined with one or more chemotherapy (e.g. taxotere; and AZD1839; col. 43, line 21 to col. 58) to treat solid tumors in human and the reference claims are also directed to a combination comprising quinazoline derivative compound (e.g. AZD2171). Hence, one would reasonably expect to successfully substitute the AZD1839 component of the reference claims with taxotere as taught by Ple and combine it with AZD2171 since both the reference claims and Ple are directed to combinations comprising an anti-tumor quinazoline compound. Besides, it is routine in the oncology art to use combination of chemotherapy comprising different drugs for treating cancers in order to reduce the potential for the development of cancer resistant cells to the chemotherapy.

For the reasons stated above, claims 10 and 19-23 are deemed to be obvious variants of the limitations of the claimed subject matter of the above cited copending applications in view of Ple.

Claims 10, 19, and 21-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11 of copending application 11/663,912 in view of Ple (US Patent 7,462,623), and further in view of Zeldis (US Patent 7,468,363).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

It is noted that the reference claims are directed to compositions comprising AZD2171, or a pharmaceutically acceptable salt thereof, in combination with imatinib and a pharmaceutically acceptable carrier or excipient. Unlike the instant claims, the reference claims are not directed to combinations comprising taxane compounds (i.e. taxotere).

The above discussion of Ple is incorporated by reference. However, Ple does not teach imatinib.

Zeldis teach small molecule anti-cancer drugs, including docetaxel (col. 15, line 2) and imatinib (col. 15, line 15-16).

It would have been obvious to a person of skill in the art at the time the invention was made to manipulate the reference combination of AZD2171 and imatinib by substituting the imatinib with any suitable conventionally known chemotherapy (e.g. taxotere) as taught by Ple (col. 43, line 44) to arrive at the instant claimed invention (AZD2171 in combination with taxotere) for use in treating solid tumors in humans. One would have been motivated to do so because Zeldis suggest that docetaxel and imatinib are equivalent small molecule anti-cancer drugs. Further, Ple suggest that quinoazoline derivative compounds with anti-tumor activity can be combined with one or more chemotherapy (e.g. taxotere) to treat solid tumors in human and the reference claims are also directed to a combination comprising a quinazoline derivative compound (e.g.

AZD2171) and a chemotherapy agent (e.g. imatinib). Hence, one would reasonably expect to successfully substitute the imatinib component of the reference claims with taxotere as taught by Ple and combine it with AZD2171 since both the reference claims and Ple are directed to combinations comprising an anti-tumor quinazoline compound and another chemotherapy drug. Besides, it is routine in the oncology art to use combination of chemotherapy comprising different drugs for treating cancers in order to reduce the potential for the development of cancer resistant cells to the chemotherapy.

For the reasons stated above, claims 10 and 19-23 are deemed to be obvious variants of the limitations of the claimed subject matter of the above cited copending applications in view of Ple, and further in view of Zeldis.

Claims 10, 19, 21-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 13-14 of copending application 11/994,824, in view of Ple (US Patent 7,462,623), and further in view of of Zeldis (US Patent 7,468,363).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

It is noted that the reference claims are directed to compositions comprising AZD2171 in combination with gemcitabine and a pharmaceutically acceptable carrier or excipient. Unlike the instant claims, the reference claims are not directed to combinations comprising taxane compounds (i.e. taxotere).

The above discussion of Ple is incorporated by reference. However, Ple does not teach gemcitabine.

Zeldis teach small molecule anti-cancer drugs, including docetaxel (col. 15, line 2) and gemcitabine (col. 15, line 12-13).

It would have been obvious to a person of skill in the art at the time the invention was made to manipulate the reference combination of AZD2171 and gemcitabine by substituting the gemcitabine with any suitable conventionally known chemotherapy (e.g. taxotere) as taught by Ple (col. 43, line 44) to arrive at the instant claimed invention (AZD2171 in combination with taxotere) for use in treating solid tumors in humans. One would have been motivated to do so because Zeldis suggest that docetaxel and gemcitabine are equivalent small molecule anti-cancer drugs. Further, Ple suggest that quinoazoline derivative compounds with anti-tumor activity can be combined with one or more chemotherapy (e.g. taxotere) to treat solid tumors in human and the reference claims are also directed to a combination comprising a quinazoline derivative compound (e.g. AZD2171) and a chemotherapy agent (e.g. gemcitaine). Hence, one would reasonably expect to successfully substitute the gemcitaine omponent of the reference claims with taxotere as taught by Ple and combine it with AZD2171 since both the reference claims and Ple are directed to combinations comprising an anti-tumor quinazoline compound and another chemotherapy drug. Besides, it is routine in the oncology art to use combination of chemotherapy comprising different drugs for treating cancers in order to reduce the potential for the development of cancer resistant cells to the chemotherapy.

For the reasons stated above, claims 10 and 19-23 are deemed to be obvious variants of the limitations of the claimed subject matter of the above cited copending applications in view of Ple, and further in view of Zeldis.

These rejections are provisional obviousness-type double patenting rejections because the conflicting claims of the copending applications have not in fact been patented.

Response to applicant's arguments

Regarding copending application 10/594,235 , this rejection is withdrawn in view of the cancellation of the conflicting claim 17.

Regarding copending application 10/594,233, this rejection is withdrawn in view of the cancellation of the conflicting claims 9 and 11.

In addition, Applicant's request to hold the nonstatutory obviousness-type double patenting rejections in abeyance pending a finding of allowable subject matter is acknowledged. However, since applicant has not substantially traversed the rejections, the rejections are maintained for the reasons of record.

Relevant Art of Record

The below cited art made of record and relied upon are considered pertinent to applicant's invention.

Zasloff et al. (US Patent 6,596,712) teach that antiangiogenic agents are particularly useful in combination because they are not likely to cause resistance development since they do not act on the tumor, but on normal host tissue (see col. 2,

line 36 to col. 3, line 6, especially col. 3, lines 3-6). Zasloff et al. also teach that combination of drugs with different mechanism of action is an accepted method of treatment which prevents development of resistance by the treated tumor (col. 2, line 65 to col. 3, line 3). Zasloff et al. suggest that addition of an angiogenesis inhibitor may be beneficial in combination with a platinum agent and a taxane such as docetaxel for treating advanced ovarian cancer (col. 4, lines 1-25).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like

assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

6 April 2008

/C. R./

Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611